

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1.- 11. (Cancel)

12. (Currently amended) A method of treating, preventing, or ameliorating an immune system disease or disorder, comprising administering to an animal in which such treatment, prevention, or amelioration is desired, a [[BLYS]]BLSP binding polypeptide in an amount effective to treat, prevent, or ameliorate the immune system disease or disorder, wherein the BLSP binding polypeptide comprises an amino acid sequence selected from the group consisting of:

(1) Asp-Xaa-Leu-Thr (SEQ ID NO:446), wherein Xaa is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala;

(2) X₁-X₂-X₃-Cys-X₅-Phe-X₇-Trp-Glu-Cys-X₁₁-X₁₂-X₁₃ (SEQ ID NO:1),
wherein

X₁ is Ala, Asn, Lys, or Ser;

X₂ is Ala, Glu, Met, Ser, or Val;

X₃ is Ala, Asn, Lys, or Pro;

X₅ is Phe, Trp, or Tyr;

X₇ is Pro or Tyr;

X₁₁ is Ala, Gln, His, Phe, or Val;

X₁₂ is Asn, Gln, Gly, His, Ser, or Val; and

X₁₃ is Ala, Asn, Gly, Ile, Pro, or Ser;

(3) X₁-X₂-X₃-Cys-X₅-X₆-X₇-X₈-X₉-X₁₀-Cys-X₁₂-X₁₃-X₁₄ (SEQ ID NO:2),
wherein

X₁ is Ala, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, Val, or is absent;

X₂ is Ala, Asn, Asp, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val;

X₃ is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Trp, Tyr, or Val;

X₅ is Asp, Ile, Leu, or Tyr;

X₆ is Arg, Asp, Glu, His, Ile, Leu, Lys, Phe, Pro, Tyr, or Val;

X₇ is His, Leu, Lys, or Phe;

X₈ is Leu, Pro, or Thr;

X₉ is Arg, Asn, Gly, His, Ile, Lys, Met, or Trp;

X₁₀ is Ala, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Ser, Trp, Tyr, or Val;

X₁₂ is Asp, Gln, Glu, Gly, Ile, Leu, Lys, Phe, Ser, Trp, Tyr, or Val;

X₁₃ is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val; and

X₁₄ is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Phe, Pro, Trp, Tyr, Val, or is absent;

(4) X₁-X₂-X₃-Cys-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-Cys-X₁₃-X₁₄-X₁₅ (SEQ ID NO:3),

wherein

X₁ is Ala, Arg, Asn, Asp, Leu, Lys, Phe, Pro, Ser, or Thr;

X₂ is Asn, Asp, Gln, His, Ile, Lys, Pro, Thr, or Trp;

X₃ is Ala, Arg, Asn, Gln, Glu, His, Phe, Pro, or Thr;

X₅ is Asn, Asp, Pro, Ser, or Thr;

X₆ is Arg, Asp, Ile, Leu, Met, Pro, or Val;

X₇ is Ala, Ile, Leu, Pro, Thr, or Val;

X₈ is Asn, His, Ile, Leu, Lys, Phe, or Thr;

X₉ is Asn, Glu, Gly, His, Leu, Lys, Met, Pro, or Thr;

X₁₀ is Arg, Asn, Asp, Gln, Glu, Gly, Ile, Lys, Met, Pro, Ser, or Trp;

X₁₁ is Arg, Glu, Gly, Lys, Phe, Ser, Trp, or Tyr;

X₁₃ is Gln, Glu, Ile, Leu, Phe, Pro, Ser, Tyr, or Val;

X₁₄ is Asn, Gly, Ile, Phe, Pro, Thr, Trp, or Tyr; and

X₁₅ is Asn, Asp, Glu, Leu, Lys, Met, Pro, or Thr;

(5) X₁-X₂-X₃-Cys-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-X₁₂-Cys-X₁₄-X₁₅-X₁₆ (SEQ ID NO:4),

wherein

X₁ is Asn, Asp, His, Leu, Phe, Pro, Ser, Tyr, or is absent;

X₂ is Arg, Asn, Asp, His, Phe, Ser, or Trp;

X₃ is Asn, Asp, Leu, Pro, Ser, or Val;

X₅ is Asp, Gln, His, Ile, Leu, Lys, Met, Phe, or Thr;

X₆ is His, Ile, Leu, Met, Phe, Pro, Trp, or Tyr;

X₇ is Asp, His, Leu, or Ser;

X₈ is Ala, Arg, Asp, Glu, Leu, Phe, Pro, or Thr;

X₉ is Ala, Arg, Asn, or Leu;

X₁₀ is Ile, Leu, Met, Pro, Ser, or Thr;

X₁₁ is Ala, Arg, Asn, Gly, His, Lys, Ser, or Tyr;

X₁₂ is Ala, Arg, Asn, Gln, Leu, Met, Ser, Trp, Tyr, or Val;

X₁₄ is Asp, Gly, Leu, Phe, Tyr, or Val;

X₁₅ is Asn, His, Leu, Pro, or Tyr; and

X₁₆ is Asn, Asp, His, Phe, Ser, or Tyr;

(6) X₁-X₂-X₃-Cys-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-X₁₂-X₁₃-X₁₄-Cys-X₁₆-X₁₇-X₁₈ (SEQ ID NO:5),

wherein

X₁ is Arg, Asp, Gly, His, Leu, Phe, Pro, Ser, Trp, Tyr, or is absent;

X₂ is Ala, Arg, Asn, Asp, Gly, Pro, Ser, or is absent;

X₃ is Arg, Asn, Gln, Glu, Gly, Lys, Met, Pro, Trp or Val;

X₅ is Arg, Asn, Gln, Glu, His, Leu, Phe, Pro, Trp, Tyr, or Val;

X₆ is Arg, Asp, Gln, Gly, Ile, Lys, Phe, Thr, Trp or Tyr;

X₇ is Ala, Arg, Asp, Glu, Gly, Leu, Ser, or Tyr;

X₈ is Asp, Gln, Glu, Leu, Met, Phe, Pro, Ser, or Tyr;

X₉ is Asp, Leu, Pro, Thr, or Val;

X₁₀ is Arg, Gln, His, Ile, Leu, Lys, Met, Phe, Thr, Trp or Tyr;

X₁₁ is Ala, Arg, Asn, Gln, Glu, His, Leu, Lys, Met, or Thr;

X₁₂ is Ala, Asn, Gln, Gly, Leu, Lys, Phe, Pro, Thr, Trp, or Tyr;

X₁₃ is Ala, Arg, Gln, His, Lys, Met, Phe, Pro, Thr, Trp, or Tyr;

X₁₄ is Arg, Gln, Glu, Gly, His, Leu, Met, Phe, Pro, Ser, Thr, Tyr, or Val;

X₁₆ is Arg, Asp, Gly, His, Lys, Met, Phe, Pro, Ser, or Trp;

X₁₇ is Arg, Asn, Asp, Gly, His, Phe, Pro, Ser, Trp or Tyr; and

X₁₈ is Ala, Arg, Asn, Asp, His, Leu, Phe, or Trp;

(7) X₁-X₂-X₃-X₄-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-X₁₂ (SEQ ID NO:6),

wherein

X₁ is Ala, Arg, Gly, His, Leu, Lys, Met, Phe, Trp, Tyr, or Val;

X₂ is Ala, Arg, Gln, His, Ile, Leu, Phe, Thr, Trp, or Tyr;

X₃ is Ala, Asp, Lys, Phe, Thr, Trp or Tyr;

X₄ is Arg, Asp, Gln, Lys, Met, Phe, Pro, Ser, Tyr, or Val;

X₅ is Asp, Leu, Lys, Phe, Pro, Ser, or Val;

X₆ is His, Ile, Leu, Pro, Ser, or Thr;

X₇ is Arg, Gly, His, Leu, Lys, Met, or Thr;

X₈ is Ala, Arg, Asn, Ile, Leu, Lys, Met, or Thr;

X₉ is Ala, Asn, Arg, Asp, Glu, Gly, His, Leu, Met, Ser, Trp, Tyr, or Val;

X₁₀ is Ile, Leu, Phe, Ser, Thr, Trp, Tyr, or Val;

X₁₁ is Ala, Arg, Gly, His, Ile, Leu, Lys, Pro, Ser, Thr, Trp, Tyr, or Val; and

X₁₂ is Arg, Asp, His, Leu, Lys, Met, Phe, Pro, Ser, Trp, Tyr, or Val;

(8) X₁-X₂-X₃-X₄-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-X₁₂-X₁₃ (SEQ ID NO:7),

wherein

X₁ is Asp, Gln, Glu, Gly, His, Lys, Met, or Trp;

X₂ is Arg, Gln, His, Ile, Leu, or Pro;

X₃ is Asp, Gly, Ile, Lys, Thr, Tyr or Val;

X₄ is Asn, Asp, Gln, Glu, Met, Pro, Ser, or Tyr;

X₅ is Asn, Asp, His, Ile, Leu, Met, Pro, Thr or Val;

X₆ is Asp, Glu, His, Leu, Lys, Pro, or Val;

X₇ is Arg, Asn, Gln, His, Ile, Leu, Met, Pro, or Thr;

X₈ is Gln, Gly, His, Leu, Met, Ser, or Thr;

X₉ is Asn, Gln, Gly, His, Leu, Lys, Ser, or Thr;

X₁₀ is Ala, Gly, Ile, Leu, Lys, Met, or Phe;

X₁₁ is Ala, Glu, His, Ile, Leu, Met, Ser, Thr, Trp, Tyr, or Val;

X₁₂ is Arg, Gln, Glu, Gly, His, Ile, Lys, Tyr, or Val; and

X₁₃ is Arg, Asn, Glu, His, Ile, Ser, Thr, Trp, or Val;

(9) Cys-X₂-Phe-X₄-Trp-Glu-Cys (SEQ ID NO:8),

wherein

X₂ is Phe, Trp, or Tyr; and

X₄ is Pro or Tyr;

(10) Cys-X₂-X₃-X₄-X₅-X₆-X₇-Cys (SEQ ID NO:9),

wherein

X₂ is Asp, Ile, Leu, or Tyr;

X₃ is Arg, Asp, Glu, His, Ile, Leu, Lys, Phe, Pro, Tyr, or Val;

X₄ is His, Leu, Lys, or Phe;

X₅ is Leu, Pro, or Thr;

X₆ is Arg, Asn, Gly, His, Ile, Lys, Met, or Trp; and

X₇ is Ala, Asn, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Ser, Trp, Tyr, or Val;

(11) Cys-X₂-X₃-X₄-X₅-X₆-X₇-X₈-Cys (SEQ ID NO:10),

wherein

X₂ is Asn, Asp, Pro, Ser, or Thr;

X₃ is Arg, Asp, Ile, Leu, Met, Pro, or Val;

X₄ is Ala, Ile, Leu, Pro, Thr, or Val;

X₅ is Asn, His, Ile, Leu, Lys, Phe, or Thr;

X₆ is Asn, Glu, Gly, His, Leu, Lys, Met, Pro, or Thr;

X₇ is Arg, Asn, Asp, Gln, Glu, Gly, Ile, Lys, Met, Pro, Ser, or Trp; and

X₈ is Arg, Glu, Gly, Lys, Phe, Ser, Trp, or Tyr;

(12) Cys-X₂-X₃-X₄-X₅-X₆-X₇-X₈-X₉-Cys (SEQ ID NO:11),

wherein

X₂ is Asp, Gln, His, Ile, Leu, Lys, Met, Phe, or Thr;

X₃ is His, Ile, Leu, Met, Phe, Pro, Trp, or Tyr;

X₄ is Asp, His, Leu, or Ser;

X₅ is Ala, Arg, Asp, Glu, Leu, Phe, Pro, or Thr;

X₆ is Ala, Arg, Asn, or Leu;

X₇ is Ile, Leu, Met, Pro, Ser, or Thr;

X₈ is Ala, Arg, Asn, Gly, His, Lys, Ser, or Tyr; and

X₉ is Ala, Arg, Asn, Gln, Leu, Met, Ser, Trp, Tyr, or Val;

(13) Cys-X₂-X₃-X₄-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-Cys (SEQ ID NO:12),

wherein

X₂ is Arg, Asn, Gln, Glu, His, Leu, Phe, Pro, Trp, Tyr, or Val;

X₃ is Arg, Asp, Gln, Gly, Ile, Lys, Phe, Thr, Trp or Tyr;

X₄ is Ala, Arg, Asp, Glu, Gly, Leu, Ser, or Tyr;

X₅ is Asp, Gln, Glu, Leu, Met, Phe, Pro, Ser, or Tyr;

X₆ is Asp, Leu, Pro, Thr, or Val;

X₇ is Arg, Gln, His, Ile, Leu, Lys, Met, Phe, Thr, Trp or Tyr;

X₈ is Ala, Arg, Asn, Gln, Glu, His, Leu, Lys, Met, or Thr;

X₉ is Ala, Asn, Gln, Gly, Leu, Lys, Phe, Pro, Thr, Trp, or Tyr;

X₁₀ is Ala, Arg, Gln, His, Lys, Met, Phe, Pro, Thr, Trp, or Tyr; and

X₁₁ is Arg, Gln, Glu, Gly, His, Leu, Met, Phe, Pro, Ser, Thr, Tyr, or Val;

(14) Ala-X₂-X₃-X₄-Asp-X₆-Leu-Thr-X₉-Leu-X₁₁-X₁₂-X₁₃-X₁₄ (SEQ ID NO:447),

wherein

X₂ is Asn, Ser, Tyr, Asp, Phe, Ile, Gln, His, Pro, Lys, Leu, Met, Thr, Val, Glu, Ala, Gly, Cys, or Trp;

X₃ is Trp, Glu, Lys, Cys, Leu, Ala, Arg, Gly, or Ser;

X₄ is Tyr, Phe, Glu, Cys, Asn;

X₆ is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala;

X₉ is Lys, Asn, Gln, Gly, or Arg;

X₁₁ is Trp, Ser, Thr, Arg, Cys, Tyr, or Lys;

X₁₂ is Leu, Phe, Val, Ile, or His;

X₁₃ is Pro, Leu, His, Ser, Arg, Asn, Gln, Thr, Val, Ala, Cys, Ile, Phe, or Tyr; and

X₁₄ is Asp, Glu, Asn, Val, His, Gln, Arg, Gly, Ser, Tyr, Ala, Cys, Lys, Ile, Thr or Leu; and

(15) X₁-X₂-Asp-X₄-Leu-Thr-X₇-Leu-X₉-X₁₀ (SEQ ID NO:448),

wherein

X₁ is Trp, Glu, Lys, Cys, Leu, Ala, Arg, Gly, or Ser;

X₂ is Tyr, Phe, Glu, Cys, Asn;

X₄ is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala;

X₇ is Lys, Asn, Gln, Gly, or Arg;

X₉ is Trp, Ser, Thr, Arg, Cys, Tyr, or Lys; and

X₁₀ is Leu, Phe, Val, Ile, or His.

13. (Original) The method of claim 12, wherein the immune system disease or disorder is an autoimmune disease or disorder.

14. (Withdrawn) The method of claim 12, wherein the immune system disease or disorder is an immunodeficiency.

15. (Original) The method of claim 13, wherein the autoimmune disease or disorder is lupus.

16. (Withdrawn) The method of claim 12, wherein the immune system disease or disorder is glomerular nephritis, rheumatoid arthritis, multiple sclerosis, hypogammaglobulinemia, hypergammaglobulinemia, or graft vs. host disease.

17.- 30. (Cancel)

31. (Currently amended) ~~A method of inhibiting or reducing activation of B cells, comprising contacting an effective amount of BLyS binding polypeptide with BLyS,~~ The method of claim 12, wherein the effective amount of [[BLyS]]BLSP binding polypeptide inhibits or reduces [[BLyS]]BLSP mediated B cell activation.

32. (Currently amended) ~~A method of inhibiting or reducing activation of B cells, comprising administering to an animal in which such inhibition or reduction is desired, a BLyS binding polypeptide in an amount effective to~~ The method of claim 12, wherein the effective amount of BLSP binding polypeptide inhibits or reduces B cell activation.

33.- 69. (Cancel)

70. (Currently amended) The method of claim 12~~according to claim 69~~, wherein the BLSP[[BLyS]] binding polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 20-168 and 186-435, as depicted in Tables 1-8 and 13.

71. (Currently amended) The method of claim 12~~according to claim 69~~, wherein the BLSP[[BLyS]] binding polypeptide comprises an amino acid sequence selected from the group consisting of:

Ala-Gly-Lys-Glu-Pro-Cys-Tyr-Phe-Tyr-Trp-Glu-Cys-Ala-Val-Ser-Gly (SEQ ID NO:450);

Ala-Gly-Val-Pro-Phe-Cys-Asp-Leu-Leu-Thr-Lys-His-Cys-Phe-Glu-Ala-Gly (SEQ ID NO:451);

Gly-Ser-Ser-Arg-Leu-Cys-His-Met-Asp-Glu-Leu-Thr-His-Val-Cys-Val-His-Phe-Ala-Pro (SEQ ID NO:452);

Gly-Asp-Gly-Gly-Asn-Cys-Tyr-Thr-Asp-Ser-Leu-Thr-Lys-Leu-His-Phe-Cys-Met-Gly-Asp-Glu (SEQ ID NO:453);

Gly-Tyr-Asp-Val-Leu-Thr-Lys-Leu-Tyr-Phe-Val-Pro-Gly-Gly (SEQ ID NO:454);

Trp-Thr-Asp-Ser-Leu-Thr-Gly-Leu-Trp-Phe-Pro-Asp-Gly-Gly (SEQ ID NO:455);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:186);

Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:456);

Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu (SEQ ID NO:457);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Val (SEQ ID NO:189);

Ala-Asn-Trp-Phe-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:309);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Ser-Leu-Pro-Asp (SEQ ID NO:458);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Phe-Pro-Asp (SEQ ID NO:353); and

Ala-Asn-Trp-Tyr-Asp-Ser-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:327).

72. (New) The method of claim 12, wherein the BLSP binding polypeptide is fused to a heterologous polypeptide.

73. (New) The method of claim 72, wherein the BLSP binding polypeptide is fused to an Immunoglobulin Fc.

74. (New) The method of claim 72, wherein the BLSP binding polypeptide is fused to human serum albumin (HSA).

75. (New) The method of claim 12, wherein the BLSP binding polypeptide is about 6 to less than about 60 amino acid residues in length.

76. (New) The method of claim 75, wherein the BLSP binding polypeptide is fused to a heterologous polypeptide.

77. (New) The method of claim 75, wherein the BLSP binding polypeptide is about 6 to less than about 20 amino acid residues in length.

78. (New) The method of claim 12, wherein the BLSP binding polypeptide interferes with the interaction between BLSP and a BLSP receptor.

79. (New) The method of claim 72, wherein the BLSP binding polypeptide interferes with the interaction between BLSP and a BLSP receptor.

80. (New) The method of claim 12, wherein the subject is human.

81. (New) The method of claim 12, wherein the amount is effective to inhibit or reduce immunoglobulin production.

82. (New) The method of claim 12, wherein the amount is effective to inhibit or reduce B cell proliferation or activation.

83. (New) The method of claim 12, wherein the BLSP binding polypeptide comprises SEQ ID NO:446.

84. (New) The method of claim 83, wherein Xaa of SEQ ID NO:446 is Pro.

85. (New) The method of claim 83, wherein the BLSP binding polypeptide comprises SEQ ID NO:448.

86. (New) A method of treating, preventing, or ameliorating lupus, comprising administering to an animal in which such treatment, prevention, or amelioration is desired, a BLSP binding polypeptide in an amount effective to treat, prevent, or ameliorate lupus, wherein the BLSP binding polypeptide comprises Asp-Xaa-Leu-Thr (SEQ ID NO:446), wherein Xaa is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala.

87. (New) The method of claim 86, wherein Xaa of SEQ ID NO:446 is Pro.

88. (New) The method of claim 86, wherein the BLSP binding polypeptide comprises SEQ ID NO:448.

89. (New) The method of claim 86, wherein the subject is human.